Effect of fasting plasma glucose on serum creatinine, urinary creatinine and urinary microalbumin in type 2 diabetics

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Abstract - Diabetes mellitus is the leading cause of end-stage renal disease (ESRD) and accounts for 30–50% of incident ESRD cases. Maintaining tight glycaemic control is important for prevention in end-stage renal disease patients with diabetic mellitus. This study was aimed to evaluate the effect of fasting plasma glucose (FPG) on serum creatinine, urinary creatinine and urinary microabumin in Type 2 diabetic patients attending Diabetic Center, Teaching Hospital, Jaffna. A total of 98 patients diagnosed as type 2 diabetics without chronic kidney diseases were included. FPG (Glucose Oxidase method), serum and urine creatinine (Jaffe Alkaline Picric Acid method) and random urine albumin (Immuno-turbidimetry method) were estimated. The strength of correlation was determined by Pearson correlation. The mean FPG, serum creatinine, urine albumin, urine creatinine and urine albumin to creatinine ratio were 136.17 (±53.92) mg/dL, 1.25 (±0.64) mg/dL, 18.9 (±16.2) mg/L, 1.21 (±0.80) g/L and 17.11 (±14.16) mg/g creatinine respectively. The association between the FPG and serum creatinine level was not significant (Pearson Chi-Square=1.99; p=0.37). Similar finding was observed for urine creatinine. Among the patients with albuminuria, 15% (n=15) were having the FPG level >126mg/dL while only 6% (n= 6) patients with albuminuria were having FPG level <100mg/dL (glycaemic control). In this study, 16 (n=4), 32 (n=8) and 52.0% (n=13) of patients had microalbuminuria with the FPG levels of <100, 100-126 and >126mg/dL respectively. The trend of microalbuminuria category was positive with FPG (Regression trend R2=0.99). FPG level showed weak positive correlatons with serum creatinine (r= 0.107, p= 0.293), urine albumin (r = 0.424, p= 0.001) and urine creatinine (r = 0.002, p= 0.982). In contrast, FPG significantly correlated with urine creatinine ratio (r = 0.422, p= 0.001). Serum creatinine level showed non-significant correlations with urine albumin (r= 0.109, p= 0.283), urine creatinine (r= 0.138, p= 0.176) and urine albumin to urine creatinine ratio (r= 0.062, p= 0.546). This study revealed that, more than 75% of the diabetic patients were having poor glycaemic control and their serum and urine creatinine and urinary albumin levels were elevated. Poor glycaemic control leads to failure in renal functions. The FPG could be used to predict the excretion of albumin and early renal diseases in diabetic patients. However, the effects of duration of diabetes and the prolonged elevation of plasma glucose levels have to be studied to find their effect on albumin excretion.

Keywords - Creatinine, Glycaemic control, Microalbuminuria, Type 2 Diabetes.

INTRODUCTION

Insufficient production of insulin by β- cells of Langerhans or the insulin resistance lead to type 2 diabetes mellitus[1]. Diabetes mellitus may cause severe cardiovascular, neurological, retinal and renal complications and chronic metabolic disorders [2]. According to the International Diabetes Federation, South-East Asia, estimated prevalence of diabetes in the South-East Asia Region is 78 million and it will rise to 140 million by 2040. In Sri Lanka, there were 1.16 million (8.5%) diabetes in 2015 [5]. Thus, diabetes mellitus and its complications may be a big burden to Sri Lanka in near future and for its policy on free medical system. Due to uncontrolled blood glucose levels, the glycosylation of proteins shall increase the diabetic nephropathy and lead to kidney failure. Reduction in glomerular filtration leads to increase in serum creatinine and represents the abnormal renal function [3 & 4]. Diabetes is closely associated with microvascular disease, often manifesting as albuminuria. Glycaemic control in these patients has been shown to be associated with microvascular and macrovascular complications and mortality.

Diabetes nephropathy is a leading cause of end stage renal disease and affects 20 to 30% of diabetics [3]. Most sensitive and simplest prognostic factor is represented by microalbuminuria, which is one of the earliest sign of progressive diabetic nephropathy, increased vascular permeability and vascular function abnormality in type 2 diabetics [4]. Serum creatinine is a perfect filtration marker of glomerular filtration rate (GFR) [3] and is a sensitive indicator of renal function [4]. The aim of this study was to find the effect of fasting plasma glucose on serum creatinine, urinary creatinine and urinary microalbumin and reveal the correlation among them in type 2 diabetic patients attending Diabetic Center, Teaching Hospital, Jaffna.

METHODOLOGY

subjects

A cross sectional study was designed. Blood and urine samples of the patients who had been diagnosed to have type 2 diabetes mellitus and attending Diabetic Centre, Teaching Hospital, Jaffna were selected for this study. The sample size was 98 [5], based on the total population attending the clinic in a month. Informed written consents were obtained from the patients. Patients with fever, obstructive liver disease, thyroid disease, already diagnosed as chronic kidney disease or pyelonephritis or glomerulonephritis and on treatment, evidence of proteinuria due to other ill-health and congestive cardiac failure or history of heart failure of any stage were excluded from this study. Data extraction sheet was used to enter the details of patients such as sex, age, height and weight

were filled by the interviewer administered way. Ethical clearance was obtained from the Ethics Review Committee of the Faculty of Medicine, University of Jaffna.

ANALYTICAL METHODS

Height, weight, sex, fasting (8h) plasma glucose concentration [Glucose Oxidase, 6], serum and urine creatinine concentration (Colorimetric Jaffe Alkaline Picric Acid, 7] and urinary Microalbumin concentration (Immunoturbidimetry, 8] were measured. Data was entered in Statistical Packages for Social Sciences (SPSS) Version 21. Basic descriptive statistics named mean and standard deviation, Independent t-test, Pearson chi squared and Pearson correlation which were applied to correlate between the parameters were used.

RESULTS AND DISCUSSIONS

Out of 98 diabetics, 60 were females (61.23%). Mean age was 59.9 (±10.4) with the range of 40 to 85 years. Majority of type 2 diabetic patients [36 nos.] were in the age group of 60-69 years. It was the same age group with the highest number of both males [15 (15.31%)] and females [21 (21.43%)]. There was no significant difference in the body mass index of males [24.1 (±3.3) kg/m2] and females [25.3 (±5.2) kg/m2] (p= 0.182).

Mean FPG level was 136.17 (±53.92) [144.59 (±70.09) and 130.85 (±40.3) mg/dL in males and females respectively but did not differ significantly, (p = 0.221)], which was significantly higher than the glycaemic control based on the FPG level (<126mg/dL). However, FPG level of the 17.4, 31.6 and 51 % of the patient were <100mg/dL (controlled), 100-126 mg/dL (like that of prediabetics) and >126mg/dL (uncontrolled glycaemic control) respectively. Mean serum creatinine level was 1.25 (±0.64) mg/dL [in males and females were 1.28 (±0.72) and 1.23 (±0.59) mg/dL respectively and did not differ significantly (p= 0.714)]. Mean random urine creatinine excretion was 1.21 (±0.80) g/L [by males and females were 1.36 (±0.96) and 1.11 (±0.68) g/L respectively and not differed significantly (p=0.124)]. Mean random urine albumin excretion was 18.9 (±16.2) mg/L. Mean urine albumin to creatinine ratio was 17.11 (±14.16) mg/g creatinine.When the patients were grouped based on the FPG levels from 60 to ≥201mg/dL and majority of the patients (29 nos.) had the FPG level of 121-140mg/dL and was true for females 21 (21.43%), but not for males. Highest number of males had the FPG level of 101-120mg/dL. It was observed that the highest amount of serum creatinine level [1.49(±0.96)mg/dL] was found in the group with the FPG level ≥201mg/dL (Table 1). This was true for both males and females who had the FPG level ≥201mg/dL (Table 1).

Urine albumin excretion level increased with the increase in FPG level in type 2 diabetic patients. Urine albumin excretion [97.08(±143.79)mg/dL] increased with the increase in FPG level and was highest in the group having FPG level of ≥201mg/L (Table 1). This was true for both males [148.49 (±217.5)mg/dL] and females [58.52 (±72.1)mg/dL] having the highest urine albumin in the sub-group with FPG level ≥201 mg/L. However, in general it has been observed that males excreted more albumin than females.

Highest amount of urine creatinine excretion [1.51(±1.08) mg/L] was observed among the patients having the FPG level between 161-180mg/dL (Table 1). But this was different in males and females. In males, highest creatinine excretion [1.81(±1.61) g/L] was observed among those who had the FPG level in the range of 141-160 mg/dL while in the females, highest creatinine excretion [1.91(±1.16) g/L] was observed in those who had the FPG level in the range of 181-200mg/dL in females (Table 1). These variations between males and females in relation to the FPG levels could be due to the small number of patients with the FPG ranges of 141-160 [n=10 (10.20%)], 181-200 [n=4 (4.08%)] and ≥ 201mg/dL[n=7 (7.14%)].

Highest amount of urine albumin to creatinine ratio was 175.11(±240.52)mg/g in the patients having FPG level ≥201mg/dL (Table 1). Similar observation of highest urine albumin to creatinine ratio was found among the patients having the fasting plasma glucose level ≥201mg/L in both males [305.69(±337.47) mg/g] and females [77.19(±99.69) mg/g] (Table 1). Males showed higher urine albumin to creatinine ratio than the females. When the patients were classified based on narrow ranges of FPG level, number patients fell into certain categories were very small. Hence it was decided to classify the type 2 diabetic patients into those having <100mg/dL, 100-126mg/dL and ≥126mg/dL (Table 2)[9]. It has been observed that most of the patients [no=50 (51.02%)] were having the FPG level more than 126mg/dL and the same is true for males and females (Table 2).

The highest serum creatinine (1.28vs1.078; p=0.245), urine creatinine (1.28vs0.84;p=0.045), and random urine albumin (35.29vs29.73; p=0.709) were observed among the patients having FPG level ≥100mg/dL when compared with the patients who hadthe FPG <100mg/dL except urine albumin to creatinine ratio (45.13vs 70.68; p=0.365). Similar results were observed in both males (except the males who showed highest amount of random urine creatinine in the group having the fasting plasma glucose level of 100-126mg/dL) and females.

In this study 51% (n=50) of the patients had hypercreatinaemia (>1.3 mg/dL for males and >1.1 mg/dLfor females). Among the hypercreatinaemic patients, 56 (n=28), 32 (n=16) and 12% (n=6) of patients had FPG of <100, 100-126, >126mg/dL respectively. The association between the FPG and serum creatinine level was not significant (Pearson Chi-Square=1.99; p=0.37). Similar trend was observed with urine creatinine. Only 24.5% (n=24) of the patients excreted high amount of creatinine in urine though 51% of the patients had high serum creatinine level. The association between the FPG and urine creatinine level was not significant (Pearson Chi-Square=1.49; p=0.47). In this study, 15%(n=15) of the patients had albuminuria and those were having FPG level above 126mg/dLwhile only6% (n= 6) of the patients who has FPG level <100mg/dL (glycaemic control) had albuminuria.

Among the patients, 25.5 (n=25) and 4.1% (n=4) were affected with microalbuminuria and macroalbuminuria respectively. Further, among the patients with <100, 100-126 and >126mg/dL FPG level, 16 (n=4), 32 (n=8) and 52% (n=13) had microalbuminuria respectively. The trend

of microalbuminuria was positive with the FPG category (Regression trend R2=0.99). Even though, 50% of the patients were not having glycaemic control (>126mg/dL), 4.1% of the patients were affected with macroalbuminuria. In contrast, 25.5% (n=25) of patients were affected with microalbuminuria, which is the good predictor for kidney damage. However, among the patients who had elevated FPG (>126mg/dL), 26.5 (n=163) and 4.1% (n=4) were affected with microalbuminuria and microalbuminuria respectively. On applying Pearson correlation, there was a weak positive non- significant correlation between FPG and serum creatinine (r=0.107, p=0.293) and was true in males (r=0.032, p=0.849) and females (r=0.202, p=0.121). FPG showed significant positive correlation with urine albumin (r=0.424 and p=0.001) and was true in males (r=0.490, p=0.002) while it was non-significant in females (r=0.220, p=0.091). FPG did not correlate with urine creatinine (r=0.002, p=0.982) and showed weak negative non-significant correlation in males (r=0.101, p=0.546) and non- significant weak positive correlation in females (r=0.111, p=0.399). FPG positively correlated with urine albumin creatinine ratio (r=0.422, p=0.001) and showed moderate positive significant correlation in males (r=0.520, p=0.001) while weak positive non- significant correlated in females (r=0.156 and p=0.234). In the patients, serum creatinine level showed weak positive non- significant correlations with urine albumin (r=0.109, p=0.283), urine creatinine (r=0.138, p=0.176) and urine albumin to urine creatinine ratio (r=0.062, p=0.546). In males Serum creatinine level showed non- significant weak positive correlation with urine albumin (r=0.183, p=0.271), urine creatinine (r=0.152, p=0.362) and urine albumin to urine creatinine ratio (r=0.124,p=0.458) and in females serum creatinine level showed non- significant correlations with urine albumin (r=-0.022, p=0.865) which was weak negative, urine creatinine (r=0.115, p=0.382) which was weak positive and urine albumin to random urine creatinine ratio (r=-0.05,p=0.703) which was weak negative. Urine creatinine level showed weak negative non- significant correlation with urine albumin (r=-0.051, p=0.615) while correlated significantly with urine albumin to urine creatinine ratio (r=-0.307, p=0.002). In males urine creatinine level showed weak negative non-significant correlation with urine albumin (r=-0.110, p=0.511] and significant urine albumin to urine creatinine ratio (r=-0.388,p=0.016) in females showed weak-negative non- significant correlation with urine albumin (r=-0.054, p=0.681) and urine albumin to urine creatinine ratio significantly (r=-0.286, p= 0.027). Urine albumin had strong positive significant correlation with urine albumin to random urine creatinine ratio (r=0.847, p< 0.001). Urine albumin had strong positive significant correlation with urine albumin to urine creatinine ratio in males (r=0.831, p< 0.001) and females (r=0.873, p< 0.001).

DISCUSSION

Bamanikaret al.[3] reported the mean (±SD) FPG as 133.88 (±68.99) mg/dL. Similar observation was made in our study (136.17 (±53.92) mg/dL). Several other workers reported elevated FPG levels [2]. But in our study, mean FPG level was lower than the previous findings. This is mainly due to the close monitoring of the patients at the Diabetic Centre.

There was no statistically significant difference in the FPG level of both sexes. Similar non-significant variations were reported in other studies [2 & 3]. The mean serum creatinine concentration in males (1.28 (±0.72) mg/dL) and females were (1.23 (±0.59) mg/dL) were higher than the reference range of serum creatinine for males and females (0.6-1.2 and 0.5-1.1 mg/dL respectively) [7].

A statistically insignificant negatively correlation was observed between creatinine clearance and microalbuminuria [9].Moderate positive correlation was observed between microalbuminuria and urine albumin to creatinine ratio (r=0.509,p=0.0006) and between urine albumin to creatinine ratio and plasma creatinine (r =0.553,p = 0.017) [10]. Similar findings were observed in this study.

CONCLUSION

This study revealed that, more than 75% of the diabetic patients were poor glycaemic control and their serum and urine creatinine and urinary albumin levels were elevated. Poor glycaemic control leads to failure in renal functions. The FPG could be used to predict the excretion of albumin and early renal diseases in diabetic patients. In contrast to that, the measurement of serum creatinine was weak positively correlated with excretion of urine albumin, urine creatinine, albumin to creatinine ratio. However, to further confirm the relationship, the effects of duration of diabetes and the prolonged elevation of plasma glucose levels have to be studied to find their effect on albumin excretion.

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Table 1: The mean (±SD) serum creatinine, random urine albumin, random urine creatinine and urine albumin to creatinine ratio of Diabetes Mellitus Type 2(males 38, females 60 and Total 98)patients grouped on their fasting plasma glucose levels.

Glucose (mg/dL)	Patients No. (%)			Serum creatinine (SD) (mg/dL)			Urine albumin (SD) (mg/L)			Urine creatinine (SD) (g/L)			Urine albumin to creatinine ratio (SD) (mg/g)		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
61-80	0 (0)	6 (6.1)	6 (6.1)	-	1.01 (0.5)	1.01 (0.45)	-	12.80 (20.1)	12.80 (8.5)	-	1.16 (0.7)	1.16 (0.71)	-	20.1 (24.9)	20.12 (24.9)
81-100	8 (8.2)	4 (4.1)	12 (12.3)	1.19 (0.4)	0.95 (0.4)	1.11 (0.39)	34.3 (62.8)	13.78 (9.9)	27.49 (51.4)	0.88 (0.5)	0.50 (0.4)	0.75 (0.51)	102.98 (181.0)	29.3 (15.2)	78.41 (149.1)
101-120	9 (9.2)	14 (14.3)	23 (23.5)	1.33 (1.0)	1.19 (0.5)	1.25 (0.73)	40.9 (51.6)	14.28 (12.3)	24.71 (35.2)	1.73 (0.9)	1.05 (0.5)	1.31 (0.73)	28.98 (35.3)	18.0 (22.9)	22.28 (28.2)
121-140	8 (8.2)	21 (21.4)	29 (29.6)	1.36 (1.1)	1.37 (0.6)	1.37 (0.77)	36.7 (45.7)	24.96 (16.8)	28.19 (27.4)	1.35 (1.0)	1.19 (0.7)	1.23 (0.77)	34.33 (60.9)	26.50 (17.9)	28.66 (34.2)
141-160	3 (3.1)	7 (7.1)	10 (10.2)	1.33 (0.4)	1.17 (0.3)	1.21 (0.31)	52.8 (27.8)	31.25 (61.9)	37.71 (53.2)	1.81 (1.6)	0.97 (0.7)	1.22 1.06)	82.0 (102.1)	74.3 (171.7)	76.62 (148.3)
161-180	5 (5.1)	2 (2.0)	7 (7.14)	1.13 (0.4)	0.99 (0.6)	1.09 (0.32)	61.1 (52.4)	18.07 (8.8)	48.79 (47.8)	1.49 (1.1)	1.56 (1.4)	1.51 (1.08)	44.90 (41.3)	23.1 (26.1)	38.67 (36.9)
181-200	2 (2.0)	2 (2.0)	4 (4.08)	1.15 (0.3)	1.10 (0.3)	1.12 (0.25)	13.8 (7.9)	26.19 (16.3)	19.99 (12.7)	0.96 (0.5)	1.91 (1.2)	1.44 (0.91)	14.17 (0.9)	19.58 (8.2)	16.9 (5.7)
≥201	3 (3.1)	4 (4.1)	7 (7.1)	1.44 (0.2)	1.52 (1.3)	1.49 (0.96)	148.5 (217.5)	58.52 (72.1)	97.08 (143.8)	1.19 (1.5)	1.07 (0.6)	1.11 (0.95)	305.7 (337.5)	77.2 (99.7)	175.1 (240.5)

Table 2:The mean (±SD) serum creatinine, random urine albumin, random urine creatinine and urine albumin to creatinine ratio of type 2 diabetic patients (38 males, 60 females and total 98) having fasting plasma glucose levels as controlled (<100 mg/dL), impaired (100-126 mg/dL) and diabetes (≥126 mg/dL) (American Diabetic Association, 2017).

Glucose (mg/dL)	Sex No. (%)			Serum creatinine (SD) (mg/dL)			Urine albumin (SD) (mg/L)			Urine creatinine (SD) (g/L)			Urine albumin to creatinine ratio (SD) (mg/g)		
	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
<100	7 (7.1)	10 (10.2)	17 (17.4)	1.22 (0.42)	0.98 (0.39)	1.08 (0.41)	3.46 (2.06)	13.2 (8.7)	9.8 (8.5)	0.79 (0.52)	0.89 (0.66)	0.85 (0.6)	5.43 (5.17)	24.19 (20.45)	17.49 (18.78)
100-126	11 (11.2)	20 (20.4)	31 (31.6)	1.27 (0.91)	1.21 (0.53)	1.23 (0.68)	36.2 (47.5)	16.24 (13.9)	23.3 (31.1)	1.73 (0.79)	1.02 (0.51)	1.27 (0.7)	25.18 (32.7)	20.73 (21.64)	22.31 (25.65)
>126	20 (20.4)	30 (30.6)	50 (51.0)	1.31 (0.72)	1.33 (0.67)	1.32 (0.68)	60.44 (89.6)	31.35 (40.1)	42.99 (65.4)	1.36 (1.08)	1.24 (0.77)	1.29 (0.9)	83.98 (155.7)	43.60 (89.02)	59.75 (120.37)